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FINAL REPORT

Office of Naval Research - Department of the Navy

Contract No. Nonr-3306(00)

NR 103-510

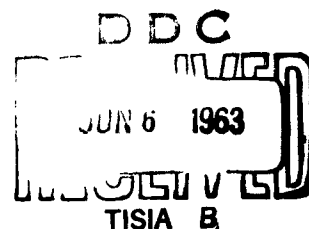
covering period Oct. 1, 1960 to Sept. 30, 1961

**"Studies on Bodily Defense Mechanisms
with the Use of Cell Cultures"**

C. M. Pomerat

Pasadena Foundation for Medical Research

Pasadena, California



**Extension of Report dated June 15, 1960
covering the period from 1947 to 1960 on
Contracts N6onr-266 T.O. 5 and Nonr-1598(01)**

General Statement

Since the year 1947 until the termination of our contracts in 1961, we had used funds from the Office of Naval Research (from \$4,000 to \$10,000 per year) for studies on bodily defenses arising in the course of a broad program in the field of experimental cytology in which tissue culture technique was the central approach. Our laboratory group moved from the University of Texas Medical Branch to the Pasadena Foundation for Medical Research in the summer of 1960. The period of transition in 1960 entailed some delays in becoming established. Our present setup has developed into a very active center for cell and molecular biology. The areas of our interest under ONR sponsorship were as follows:

I. Cellular Responses to Microbial Agents

The study by Mario Fernandes and C. M. Pomerat entitled: "Cytopathogenic effects of rabies virus on nervous tissue in vitro" was published in the Zeitschrift für Zellforschung, 53: 431-437, 1961. It is a pleasure to report that Dr. Fernandes, who was attached to the Portuguese School of Veterinary Medicine in Lisbon, employing know-how which he had accumulated in our laboratory, helped materially in the development of a successful vaccine against African swine fever. He was induced to return to the Wistar Institute in Philadelphia where he has maintained his interest in the use of cell cultures for the study of neurotropic viruses.

Dr. Martha Miquel, a virologist from Buenos Aires, Argentina, came as a fellow of the Foreign Agricultural Service, U.S.D.A., to extend the studies which had been carried out with our group by Dr. Harriet Felton on the mechanism of cellular injury by Hemophilus and Staphylococcus toxins. Dr. Miquel's attack centered on the use of diphtheria toxin since this had the advantage of being obtainable in a highly purified state as compared to the multiple antigen system derived from staphylococci. She found a marked decrease of cell division in relation to the presence of toxin, but concluded that this was an indirect effect mediated through the inhibition of RNA synthesis. More important were observations on the nucleus and cytoplasm, including the demonstration with cinematography of the disruption of the spindle which could account for the abnormal chromosome behavior of cells treated with a highly purified diphtheria toxin obtained through the courtesy of Professor A. M. Pappenheimer. Important inroads on the serial course of the cytopathology induced by this substance, involving changes in the mitochondria and endoplasmic reticulum, were abandoned due to lack of funds at the termination of the contract.

II. Cytopathology of Air Pollution and Radiation

Provisional experiments in these areas which had been aided at the outset in part by funds from ONR were shifted to other contracts. We are indebted for aid which has subsequently led to the development of a biological test for air pollutants. It has been found that human

lung cell lines show population changes in the presence of noxious gases from automobile exhausts and smog, which parallel effects produced by a known carcinogenic compound. This work has opened a new avenue for the study of air pollutants, which circumvents the use of lower animals and can be performed inexpensively. It has had an important impact in motivating social agencies in supporting more effective means of controlling this potential menace to public health. We had hoped to employ this technique for the study of possible noxious gas factors in nautical installations, including submarines.

III. Pituitary Studies

As a part of our concern with studies in the field of immunity, we foresaw the possibility of developing an immunotherapeutic agent for the suppression of the production of growth-promoting hormone from the hypophysis. The program was outlined in our contract request which was to have been initiated 1 October 1961. The initial inroad consisted of mastering the technique for the cultivation of rodent, bovine, and human anterior pituitary glands. A film record was made of the destructive properties of an anti-pituitary cytotoxic serum prepared in rabbits, together with the demonstration that rabbit serum at a dilution of 1:80 was not damaging. The properties of the cytotoxic serum were shown to be species specific. With the collaboration of Doctors W. P. Lyons and T. Hayashida of the department of anatomy of the University of California School of Medicine in

San Francisco, we were on the point of extending our observations with highly purified human anti-somatotropic (STH) hormone. One of the important goals of this work would have been to develop an anti-STH factor which might have been valuable in controlling the Kimmelstiel-Wilson syndrome. In this effort we had obtained the generous cooperation of Dr. Edgar Gordon, Professor of Internal Medicine, University of Wisconsin. None of this work has been published and the project has been abandoned.

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Attention is respectfully directed to the fact that this report covers only the period from 1960 to 1961. Reference may be made to the Final Report covering the period from 1947 - 1960 under the date of June 15, 1960. In that statement an account was given of expenditures amounting to \$54,000 received during the course of 13 years of ONR support, which resulted in the publication of 34 papers.